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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,307	10/24/2003	Shalaby W. Shalaby	PC25466A	1484

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EXAMINER	
MAEWALL, SNIGDHA	
ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/693,307	SHALABY ET AL.	
	Examiner	Art Unit	
	Snigdha Maewall	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-12* is/are pending in the application.

4a) Of the above claim(s) *2,3 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Receipt of Applicant's Arguments and RCE filed on 02/28/08 is acknowledged.

Claims 2-3 and 13 have been cancelled. Claims **1 and 4-12** are under prosecution.

The rejections made under 35 USC 102 in the Office action dated 09/28/07 is hereby withdrawn in view of Applicant's Arguments and amendments to the claims.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1 and 4-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a written description rejection.**

Instant claims are generic with respect to 'bioactive agent" and have not been sufficiently described to show possession of compositions comprising the entire genus. The invention defined by the claims requires a specific type physiochemical interaction between the bioactive agent and a polymer in order to produce the desired result. With regard to the bioactive agent, the aryl-heterocyclic compounds described in US 4,831,031 (incorporated by reference into instant disclosure on page 3 of the specification) are sufficiently similar in structure or function that the showing of ziprasidone is sufficient to show possession of this sub- genus. However, this showing is not sufficient to show possession of all bioactive agents, or all aryl-heterocyclic compounds. The genus of bioactive agent, and the sub-genus of aryl-heterocyclic compound, includes materials having disparate functions and properties. These materials may be hydrophilic or hydrophobic; they may be anionic, cationic, zwitterionic, or neutral; they may have one or more of a multitude of biological functions. Clearly, the showing in the specification, which is limited to ziprasidone, is not sufficient to show possession of all such materials in the context of the invention. Additionally, applicant has amended the claim to add new limitation such as polyester carbonate, polyester carrying two or more carboxyl groups situated in medial portions off said polymer. Applicant has not provided the specific structural configuration of the polymers, in the absence of which, the structural and functional characteristics cannot be deduced. It should be noted that claims are given broadest reasonable interpretation during prosecution and the limitation are read in light of specification, however, the limitations are not incorporated

from specification. Examiner suggests reciting specific polymeric combinations and specific bioactive drugs.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1 and 4-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shalaby to (U.S. Patent No. 5,714,159) in view of Kim et al. to (U.S. Patent No. 6,232,304 B1).

Shalaby discloses a hydrogel-forming, self-solvating, absorbable polyester copolymers capable of selective, segmental association into a compliant hydrogel mass on contact with an aqueous environment (abstract). According to Shalaby, the copolymer comprises a base component, designated as "Component A". The “Component A” refers to the basic structure of the copolymers of the invention. “Component A” comprises a molecular chain having a hydrophilic block “Y” and a relatively hydrophobic polyester block “X” . The hydrophobic block/segmented polymer comprises a polyester formed by grafting a glycolide, lactide, .epsilon.-caprolactone, p-dioxanone, trimethylene carbonate or combinations thereof, onto the hydroxylic or amino groups of a hydrophilic

polymer precursor. The hydrophilic block comprises a polyoxyethylene, poly(oxyethylene-b-oxypropylene), polypeptide polyalkylene oxamate, a polysaccharide, and derivatives thereof; or a liquid, high molecular weight polyether glycol interlinked with an oxalate or succinate functionalities in linear or branched form (column 6 and 7, lines 65-67 and 1-15).
"Component A" optionally comprises carboxylic end groups which facilitates ionically binding a bioactive agent or drug (column 7, lines 19-23). The composition comprises an absorbable carrier which helps in immediate and controlled release of the bioactive drug.(column 7, lines, 30-33).

According to Shalaby a copolymer optionally comprises a bioactive agent, such a copolymer is capable of the controlled-release of a biologically active agent for modulating cellular events such as wound healing and tissue regeneration (column 6, lines 30-45). The copolymer described by Shalaby is capable of being injected into living tissues (column 6, line 57) (hence proving that the copolymer is liquid conjugate).
The hydrophobic block "X" as described above refers to absorbable polyester chain block(s) or segment(s) of variable length, which is a viscous liquid at room temperature. These hydrophobic block (s) "X "comprises, copolymeric segments of glycolide, l-lactide, trimethylene carbonate (column 8, lines 4-9).
The "Hydrophilic Block(s)" or segment (s) "Y", comprises poly(oxyethylene) (column 8, lines 17-18).

Shalaby further discloses that the length of the hydrophilic block "Y" and its weight fractions can be varied to modulate the rate of gel formation, its modulus, its water content, and diffusivity of bioactive drug (column 8, lines 23-37).
Shalaby discloses that to render "Component A" more receptive to basic drugs, its end-groups can optionally be carboxylated (column 10, lines 1-5).
"Component A" can be succinylated to provide acidic end-groups for ionic binding on the bioactive agent/drug (column 12, lines 8-10).
Shalaby further discloses that liquid compositions made of component A with or without drug or bioactive agent can form hydrogels upon contacting a liquid environment (column 12, lines 10-12). The "Component A" as disclosed in the reference, comprises an inherent viscosity at 25 degrees C in chloroform ranging between 0.03 to 0.80 dL/g and can be present as a liquid at room temperature and can be administered through a syringe needle (column 10, lines 10-17). The liquid conjugate, "Component A" in this case can combine with bioactive drugs such as calcium (column 12, lines 58-59) hence proving the ionic bond linkage between the liquid conjugate and the bioactive drug.
Shalaby to (U.S. Patent No. 5,714,159) does not specifically teach the bioactive agent such as Ziprasidone (aryl- heterocyclic compound).
Kim et al. teaches aryl- heterocyclic drug such as Ziprasidone. Kim et al. discloses that increasing drug solubility and stability through appropriate formulation can lead to therapeutic efficacy of the drug (column 1, lines 17-20). On (column 3, lines 10-27), Kim et al. discloses that ziprasidone has utility as a neruleptic drug, and is thus useful as neuroleptic/antipsychotic drug (column 3,

lines 26-30). It is due to this utility of ziprasidone, it would have been obvious to one of ordinary skilled in the art at the time the invention was made to utilize Ziprasidone in the liquid conjugate as a bioactive drug or alternately to use polymers and carboxyl-bearing polymers or carboxyl-bearing block/segment as forwarded by Shalaby, with Ziprasidone to make liquid conjugate because Ziprasidone acts as an antipsychotic as disclosed my Kim et al. Addionally, since Ziprasidone happens to be basic in nature, it would be expected for ziprasidone to form ionic bond with carboxyl-bearing polymers or block/ segment copolymers which are acidic in nature. A skilled artisan would thus have been motivated to formulate a liquid conjugate comprising Ziprasidone and absorbable polymer with one or more carboxyl group with a reasonable expectation of success.

Response to Arguments

6. Applicant's arguments filed 02/28/08 have been fully considered but they are not persuasive.

Applicant argues rejection in view of KSR and states that there is no motivation to combine the two references. In the instant case, due to the basic characteristics of Ziprasidone and the claimed polymer, a skilled artisan would have expected to form ionic conjugated product with a reasonable expectation of success. Shalaby's reference suggests ionic conjugate such as polymers with carboxyl groups and suggests being used with basic active agents. Ziprasidone comprises nitrogen with lone pair of electron; therefore, a skilled artisan would

have formulated a liquid conjugated product with an expectation of the product comprising ionic conjugation due to acidic and basic characteristics with a reasonable expectation of success. It should be noted that the motivation to combine references need not be the same as applicant's motivation. In the instant case, combination of Ziprasidone with the suggested polymers of Shalaby would have been obvious due to its utility.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Snigdha Maewall whose telephone number is (571)-272-6197. The examiner can normally be reached on Monday to Friday; 8:30 a.m. to 5:00 p.m. EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-0580.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service

Representative or access to the automated information system, call 800-786-

9199 (IN USA OR CANADA) or 571-272-1000.

/Snigdha Maewall/
Examiner, Art Unit 1612

/Gollamudi S Kishore, Ph.D/
Primary Examiner, Art Unit 1612